REMARKS

Applicants have amended their claims in order to further clarify the definition of various aspects of the present invention. Specifically, Applicants have amended claim 1 to recite that the material fluorinated is a monosaccharide or monosaccharide bonded to a base of a nucleic acid. Claims dependent on claim 1 have been amended in light of this amendment of claim 1. Claim 4, and claims dependent thereon, have been amended to recite that a monosaccharide or monosaccharide bonded to a base of a nucleic acid is fluorinated, and claim 4 has been further amended to recite that the fluorinating agent is that represented by the general formula (I).

In light of amendments to, e.g., claims 1 and 4, claims 9-12, 15-20, 22 and 23 have been cancelled without prejudice or disclaimer, and dependencies of claims 13, 14 and 21 have been amended.

In addition, Applicants are adding new claim 25 to the application. Claim 25, dependent on claim 1, further defines the monosaccharide and the monosaccharide bonded to a base of a nucleic acid, consistent with the description, e.g., in the last full paragraph on page 9 of Applicants' specification.

Applicants respectfully traverse the rejection of their claims under the first paragraph of 35 USC 112, as set forth on pages 2-6 of the Office Action mailed January 19, 2007, particularly insofar as this rejection is applicable to the claims as presently amended. Thus, Applicants have amended their claims such that the material fluorinated is a monosaccharide or monosaccharide bonded to a base of a nucleic acid. In connection therewith, note, for example, Examples 1-13 on pages 28-34 of Applicants' specification. Note also the description, for example, in the last full paragraph on page 9 of Applicants' specification. Especially in view of present amendments to the claims, it is respectfully submitted that one of ordinary skill in the

art, without undue experimentation, could determine materials which can be fluorinated according to the present invention, using a fluorinating agent as in the present claims. Even if some experimentation were necessary, such experimentation would not be undue. In this regard, it is to be noted that following guidelines in Applicants' specification, one of ordinary skill in the art could select a specific monosaccharide or monosaccharide bonded to a base for nucleic acid and a specific fluorinating agent as in the present claims, with reaction thereof to determine whether fluorination takes place. It is respectfully submitted that such experimentation is not undue, and thus requirements of the first paragraph of 35 USC 112, of an enabling disclosure, are satisfied. See In re Angstadt, 190 USPQ 214 (CCPA1976).

The contention by the Examiner in the second full paragraph on page 4 of the Office Action mailed January 19, 2007, that "it is not possible to predict beforehand which [substrates] can and cannot serve as substrates for a particular fluorinating agent" is noted. However, it is respectfully submitted that the enablement requirement of 35 USC 112, first paragraph, does not require absolute predictability. Again, it is emphasized that all one need do is react a specific fluorination agent and a specific substrate, particularly in view of the present claims reciting a monosaccharide or a monosaccharide bonded to a base of a nucleic acid as the substrate. It is respectfully submitted that such experimentation is not undue. See In re Angstadt, supra.

The additional contention by the Examiner in the sentence bridging pages 4 and 5 of the Office Action mailed January 19, 2007, is noted. The Examiner is respectfully requested to reconsider in light of the presently amended claims, which recite fluorination of a monosaccharide or a monosaccharide bonded to a base of a nucleic acid. Especially in light thereof, and noting the disclosure as a whole,

including Examples 1-13 on pages 28-34 of Applicants' specification, it is respectfully submitted that sufficient guidance is provided for the scope of the present claims.

The contention by the Examiner on page 5 of the Office Action mailed January 19, 2007, as to lack of working examples, is noted. The Examiner's attention is again respectfully directed to Examples 1-13, showing various monosaccharides. It is respectfully submitted that these Examples, particularly in light of Applicants' disclosure as a whole, provide sufficient guidance to one of ordinary skill in the art to practice the presently claimed method without undue experimentation.

Furthermore, attention is respectfully directed to, for example, claims 2, 6, 7, 8, 13, 14, 23 and 24, further defining the fluorinating agent; and claim 25, further defining the monosaccharide and monosaccharide bonded to a base of a nucleic acid. Especially with respect to these claims, it is respectfully submitted that Applicants' original disclosure is enabling for practicing the presently claimed invention, without undue experimentation, so as to satisfy the enablement requirement of the first paragraph of 35 USC 112.

Applicants respectfully traverse the rejection of various of their claims under the first paragraph of 35 USC 112, as set forth on pages 6-10 of the Office Action mailed January 19, 2007, particularly insofar as this rejection is applicable to the present claims. In this regard, it is noted that the present claims recite that the substrate fluorinated is a monosaccharide or monosaccharide bonded to a base of a nucleic acid. It is respectfully submitted that particularly as presently amended, the claims provide sufficient guidance to practice the invention as in, for example, claim 4 and claims dependent thereon.

In this regard, it is noted that the Examiner has indicated on page 6 of the Office Action mailed January 19, 2007, that the specification is enabling "for a

method of fluorination involving an active agent of formula I or II". Claim 4 has been amended to recite that the fluorinating agent is represented by the general formula (I); accordingly, it is respectfully submitted that the basis for rejection of claims under the first paragraph of 35 USC 112, as set forth on pages 6-10 of the Office Action mailed January 19, 2007, is moot.

Applicants respectfully submit that all of the claims presented for consideration by the Examiner patentably distinguish over the teachings of the documents applied by the Examiner in rejecting claims in the Office Action mailed January 19, 2007, that is, the teachings of the articles by Chirakal, et al., "Base-Mediated Decomposition of a Mannose Triflate During the Synthesis of 2-Deoxy-2-^{18}F-fluoro-D-Glucose", in Appl. Radiat.Isot. (1995), vol. 46, no. 3, pages 149-155; and by Dmowski, et al., "Dialkyl-α, α-difluorobenzylamines and dialkyl (trifluoromethyl)-amines-novel fluorinating reagents", in Journal of Fluorine Chemistry, 23 (1983), pages 219-228, under the provisions of 35 USC 102 and 35 USC 103.

It is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a method of fluorination, which includes fluorinating a monosaccharide or monosaccharide bonded to a base of a nucleic acid using the specified fluorinating agent of general formula (I), as in claims 1 and 4; and, moreover, wherein such fluorinating takes place under irradiation with at least one of microwave and electromagnetic wave having a wavelength around a microwave region (see claim 4).

Moreover, it is respectfully submitted that the teachings of the applied references would have neither disclosed nor would have suggested such method as in the present claims, having features as discussed previously in connection with independent claims 1 and 4, and, moreover, wherein the fluorinating agent is further

defined as in claims 2, 6-8, 13, 14 and 25; and/or wherein the fluorinating is performed under irradiation with microwave having a frequency of 1-30GHz (see claim 5); and/or wherein the fluorination is performed by a thermal reaction (see claim 3); and/or wherein the fluorinating is conducted in a presence of an agent accelerating a reaction (see claim 21); and/or wherein the monosaccharide or monosaccharide bonded to a base of a nucleic acid, that is to be fluorinated, is selected from the materials as in claim 25.

Fluorinated sugars, obtained by fluorinating saccharides exhibiting excellent adaptability to the human body, are actively studied for various applications, such as anticancer agents and immunosuppressants. However, introduction of fluorine atoms into a specific position of a saccharide is often difficult, since a saccharide has a plurality of active groups such as hydroxyl groups. Note, for example, the first and second full paragraphs on page 5 of Applicants' specification. In particular, it is very difficult to fluorinate a specific position of, e.g., monosaccharides or monosaccharides bonded to a base of a nucleic acid, without having an effect on protective groups thereof.

Against this background, and as a result of intensive studies by Applicants, Applicants have found that when using a specific fluorinating agent for the fluorination reaction, with the reaction being conducted thermally or under irradiation with microwave or an electromagnetic wave having a wavelength around the microwave region, the fluorination can be conducted selectively at a specific position safely, e.g., at a temperature in the range of 150-200°C. Note the last full paragraph on page 5 of Applicants' specification.

Applicants have further found that by performing such fluorination reaction while irradiating with microwave or electromagnetic wave having a wavelength around the microwave region, fluorination at a specific position can proceed highly

selectively, efficiently in a short time and safely. See the paragraph bridging pages 6 and 7 of Applicants' specification.

As will be discussed further infra, it is respectfully submitted that there is no description, and there would have been no suggestion, in the applied references, of fluorinating a monosaccharide or a monosaccharide bonded to a base of a nucleic acid, with the fluorinating agents as in the present claims. It is respectfully submitted that the monosaccharide or monosaccharide bonded to a base of a nucleic acid is a complicated compound, which differs from, for example, primary alcohols, and has at least two hydroxy groups, each of which has different reactivity to the fluorinating agent. Therefore, it is respectfully submitted that it would not have been obvious to one of ordinary skill in the art to fluorinate monosaccharides.

It is emphasized that the present Applicants have found that selective fluorination of a specific part of the monosaccharides can be achieved, through use of the fluorinating agent as in the present claims, and that such selective fluorination is achieved without any disadvantageous effects on the protective groups.

As described on pages 1 and 2 of Applicants' specification, various methods of fluorination have been proposed, including using a HF-amine complex and DAST. Note particularly the paragraph bridging pages 1 and 2, and the sole full paragraph on page 2, of Applicants' specification. However, by using the HF-amine complex, it is required to have more aggressive reaction conditions than that of the present invention, to fluorinate monosaccharides or monosaccharides bonded to a base of a nucleic acid. When DAST or, e.g., deoxo-fluor is used for fluorination, a protective group such as a methoxy group therein is shifted to a different position of the monosaccharide, or eliminated from it. Especially in view thereof, it is respectfully submitted that one of ordinary skill in the art would not have been guided to the fluorinating agent of the present invention, for fluorinating the monosaccharide or the

monosaccharide bonded to a base of a nucleic acid, and achieving the advantages that such fluorination can occur without causing such shift or elimination of a group such as, e.g., a methoxy group. Especially in view of this advantage achieved according to the present invention, it is respectfully submitted that the teachings of the applied references do not disclose, nor would have suggested, the presently claimed invention.

As to this migration of a methoxy group, attention is respectfully directed to the article by Kobayashi, et al., "Deoxyfluorination of alcohols using N-N-diethyl-α,α-difluoro-(*m*-methylbenzyl)amine", in Tetrahedron 60 (2004), pages 6923-6930, especially pages 6925 and 6926 thereof. Copies of pages 6923-6926 are enclosed.

Chirakal, et al. reports ^{19}F-NMR evidence to show the effect of F^-, CO_3^{2-} and HCO_3^- on the base-catalysed elimination of $CF_3SO_3^-$ from 1, 3, 4, 6-tetra-*O*-acetyl-2-trifluoro-methanesulphonyl-β-D-manno-pyranose. This article also reports a rapid, efficient synthesis of 2-^{18}FDG (2-deoxy-2-^{18}F-fluoro-D-glucose) using a domestic microwave oven. Note also the Results and Discussion on pages 151-154 of this article.

It is respectfully submitted that this article is directed to an investigation of base-catalysed elimination of $CF_3SO_3^-$ from a specific sugar, and would have neither taught nor would have suggested the method according to the present invention, including, inter alia, fluorinating a monosaccharide or monosaccharide bonded to a base of a nucleic acid with a specific fluorinating agent, as in the present claims, and advantages thereof as discussed previously; and/or other features of the present invention as discussed previously, and advantages thereof.

Dmowski, et al. discloses use of α,α-difluorobenzyl (dimethyl)amine (DBDA) and diethyl(trifluoromethyl)amine (DTA) as fluorinating reagents to replace hydroxyl groups in alcohols and carboxylic acids by fluorine atoms. Note especially the first

full paragraph on page 220 of this article, describing that reactions of amines DBDA and DTA with simple primary, secondary and tertiary alcohols and with carboxylic acids are reported. See also the paragraph bridging pages 223 and 225 of this article.

It is respectfully submitted that this article would have neither taught nor would have suggested such method as in the present claims, including the material fluorinated, and advantages achieved according to the present invention including selective fluorination, discussed previously.

Applicants respectfully traverse the obviousness-type double patenting rejections, both actual and provisional, set forth on pages 12 and 13 of the Office Action mailed January 19, 2007, especially insofar as these rejections are applicable to the present claims.

Thus, claims 1-3, 5 and 6 of U.S. Patent No. 7,019,173 define a fluorinating method including, inter alia, wherein the compound or material having an active group, reacted with the fluorine compound, is a primary alcohol. Note particularly claim 6 of No. 7,019,173. It is respectfully submitted that the method claimed in No. 7,019,173 would have neither taught nor would have suggested the presently claimed method, including, inter alia, wherein the material fluorinated is a monosaccharide or monosaccharide bonded to a base of a nucleic acid, and advantages achieved by fluorinating such monosaccharide or monosaccharide bonded to a base of a nucleic acid with the fluorinating agent as in the present claims.

Copending Application No. 10/591,698, filed September 5, 2006, claims a process for producing an optically active fluoro compound by reacting a fluoroamine represented by formula (I) with an optically active diol represented by formula (II). It is emphasized that for producing the optically active fluoro compound in No.

10/591,698, the fluorine compound is reacted with a specified optically active diol. It is respectfully submitted that this method as claimed in No. 10/591,698 would have neither taught nor would have suggested the presently claimed invention, including wherein a monosaccharide or monosaccharide bonded to a base of a nucleic acid is fluorinated by the specified fluorinating agent, and advantages thereof as discussed in the foregoing.

In view of the foregoing comments and amendments, reconsideration and allowance of all claims presently in the application are respectfully requested.

To the extent necessary, Applicants petition for an extension of time under 37 CFR 1.136. Authorization is herein given to charge any shortage in the fees, including extension of time fees and excess claim fees, to Deposit Account No. 01-2135 (Case No. 396.45117X00), and please credit any excess fees to such deposit account.

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

/William I. Solomon/
William I. Solomon
Registration No. 28,565

1300 North Seventeenth Street
Suite 1800
Arlington, VA 22209
Tel.: 703-312-6600
Fax.: 703-312-6666

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